REMARKS

The Office Action of September 13, 2005 has been received and reviewed. Claims 1-9 are currently pending in the application. Claims 1-9 stand rejected. Reconsideration is respectfully requested.

Rejections Under 35 U.S.C. § 101

Claims 1-9 stand rejected under 35 U.S.C. § 101 because "the claimed invention is not supported by either a specific asserted utility or a well-established utility." (*See*, Office Action of September 13, 2005, at page 2, hereinafter referred to as "Office Action"). Applicants traverse the rejection as set forth herein.

The Examiner alleges that the "instant specification fails to establish that that the disclosed polynucleotide sequences encodes an amino acid which that mediates adhesion of Neisseria cells to human cells explicitly or implicitly as putatively asserted by the instant specification." (*Id.*). In contrast, the as-filed Specification, at page 22, Example 4, clearly demonstrates OrfA-dependent modulation of the PilC mediated adhesion function. (*See*, Specification, at pages 22-23, especially at Table 1). Applicants especially direct the Examiner's attention to the line in Table 1 that is the second from the bottom and is marked "E. coli (H2560)" and the lane marked "Chang cells." As is clearly indicated therein, this strain adhered to human epithelial cells, specifically, Chang cells. Further, in the as-filed Specification, at page 23, it is disclosed that E. coli H2560 is E. coli strain HB101 with plasmid pES25 and plasmid pES25 is a pBA vector containing a genomic fragment from Neisseria gonorrhoeae of approximately 11 kb carrying the coding regions *orfA*, *orfB*, and *orfI*.

The Examiner further rejects claims 1-9 under 35 U.S.C. § 101 because "the invention as claimed herein is not supported by either a specific asserted utility or a well-established utility." (*See*, Office Action, at page 3). This allegation is clearly inconsistent with the numerous instances throughout the as-filed Specification where the usefulness and advantages of the present invention are clearly stated. Applicants direct the Examiner's attention to the first four pages of the as-filed Specification. For instance, the as-filed Specification, at page 4, states that "the technical problem of the present invention therefore is to provide proteins and DNA molecules encoding them that serve as adhesion structures for Neisseria species or contribute to the development of such structures." Furthermore, the as-filed Specification, at the same page, states the following: "This problem is solved by providing the embodiments described in the claims." These statements, especially in light of the preceding background paragraphs at pages 1-4 in the as-filed Specification, which discuss use of the present invention for raising antibodies to the encoded proteins to block adhesion as well as other uses disclosed at pages 14 and 15 of the as-filed Specification, more than adequately describe, in clear detail, the asserted utility of the present invention.

The Examiner further rejects claims 1-9 under 35 U.S.C. § 101 because "the scope of the invention as claimed encompasses any and all variants of nucleotide sequences encoding polypeptide that mediates adhesion of Neisseria cells to human cells." (*See*, Office Action, at page 3). This is an improper rejection under 35 U.S.C. § 101 because the allegation does not relate to whether or not the claimed subject matter is statutory. However, to further clarify for the Examiner the present claims, Applicants direct the Examiner's attention to claim 1, which is directed to an isolated nucleic acid encoding a lipoprotein or active fragment thereof which

mediates adhesion of Neisseria cells to human cells selected from SEQ ID NO:4, a nucleic acid having 95% sequence identity to a nucleotide sequence encoding the peptide sequence of SEQ ID NO:4 and a nucleic acid that hybridizes to a nucleic acid having a nucleotide sequence that encodes the peptide sequence of SEQ ID NO:4, under stringent conditions. This claim could not possibly be interpreted by one of ordinary skill in the art to encompass "any and all variants of nucleotide sequences encoding polypeptide that mediates adhesion of Neisseria cells to human cells" as alleged by the Examiner. Claim 1 is clearly directed to nucleic acids having a nucleotide sequence encoding the peptide sequence of SEQ ID NO:4 and related nucleic acids. Furthermore, Applicants point out that the related nucleic acids are limited in scope according to the Revised Guidelines for Written Description. (*See*, Federal Register, Vol. 66, No. 4 January 5, 2001).

The Examiner also states that "the asserted use for the claimed invention is not supported by either a specific and/or substantial utility, since no function could be ascribed to the gene product." (*See*, Office Action, at page 4). Applicants direct the Examiner's attention to the language of the presently pending claims. The presently pending claims do not recite a "use" because Applicants understand that such "use" claims are indefinite. Rather, the present claims are directed to isolated nucleic acids, vectors and host cells comprising said isolated nucleic acids. Furthermore, these isolated nucleic acids have been characterized and encode polypeptides whose function has also been characterized, as disclosed by the present as-filed Specification. (*See*, Specification, for instance, at pages 1-4, 22-23, Example 4 and Table 1).

The Examiner further states that the "instant specification does not comply with 35 U.S.C. § 101 and 112 since nebulous expressions 'biological activity' and 'biological properties'

do not contain sufficiently explicit indication of usefulness of compounds and how to use them." (*See*, Office Action, at page 4). Again, the Examiner is reminded that the present claims are not directed to methods of use, but rather nucleic acids. This is also an improper basis for a rejection under 35 U.S.C. § 101 since it is unclear whether this is really a rejection under 35 U.S.C. § 101, § 112, first paragraph, enablement, § 112, first paragraph, written description, or § 112, second paragraph. The Examiner's attention is directed to page 7 of the as-filed Specification wherein it is stated, "[f]ragments are understood to be parts of the nucleic acid molecules that are long enough to encode the protein described." (*See*, Specification, as-filed, at page 7, emphasis added). Furthermore, the Specification recites the following, "this protein possesses a biological activity that mediates the adhesion of Neisseria cells to human cells." (*See*, *Id.* at page 9). Applicants additionally direct the Examiner's attention to the parent case, which has issued as U.S. Patent No. 6,617,128 (hereinafter referred to as "Meyer et al."). Meyer et al. recites the following claim:

> 6. An isolated fragment of the nucleic acid molecule according to claim 1 encoding **a lipoprotein or biologically active fragment of said lipoprotein** that mediates adhesion of Neisseria cells to human cells from a bacteria of the genus Neisseria selected from the group consisting of
> (a) a nucleic acid molecule encoding a protein having the amino acid sequence as depicted in SEQ ID NO:7;
> (b) a nucleic acid molecule encoding a protein having the amino acid sequence depicted in SEQ ID NO:7 from amino acid residue 19 to amino acid residue 320;
> (c) a nucleic acid molecule comprising a nucleotide sequence having 95% sequence identity to
> (i) a nucleotide sequence encoding a protein comprising SEQ ID NO:7, and
> (ii) a nucleotide sequence encoding a protein having the amino acid sequence depicted in SEQ ID NO:7 from amino acid residue 19 to amino acid residue 320; and

(d) a nucleic acid molecule comprising a nucleotide sequence that hybridizes under stringent hybridization conditions of 0.2.times.SSC, 0.1% SDS and 68.degree. C. to
(i) the complement of a nucleotide sequence encoding a protein comprising SEQ ID NO:7,
(ii) the complement of a nucleotide sequence encoding a protein having the amino acid sequence depicted in SEQ ID NO:7 from amino acid residue 19 to amino acid residue 320.

(*See*, Meyer et al., claim 6, emphasis added).

Thus, the rejection under 35 U.S.C. § 101 lack support in light of the above-identified explicitly asserted utilities found in the as-filed application, and the allowed parent application.

Reconsideration and withdrawal of the rejection of claims 1-9 are respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph

Written Description

Claims 1-9 stand rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirements. (*See*, Office Action, at pages 5-8). Applicants traverse the rejections as set forth herein.

The Examiner alleges that the instant claims "are drawn to an isolated nucleic acid sequence and/or any variant thereof that encodes a lipoprotein or any fragment thereof that mediates adhesion of Neisseria cells to human cells." (*Id.*). This allegation is not correct, especially in light of as-filed claim 1, which recites the following:

"1. An isolated nucleic acid molecule encoding a lipoprotein or a biologically active fragment of said lipoprotein that mediates adhesion of Neisseria cells to human cells from a bacteria of the genus Neisseria, selected from the group consisting of

(a) a nucleic acid molecule comprising a nucleotide sequence encoding a protein comprising SEQ ID NO: 4;

(b) a nucleic acid molecule comprising a nucleotide sequence having 95% sequence identity to a nucleotide sequence encoding a protein comprising SEQ ID NO:4 due to the degeneracy of the genetic code;

(c) a nucleic acid molecule comprising a nucleotide sequence that hybridizes under stringent hybridization conditions of 0.2 X SSC, 0.1% SDS and 68°C to

(i) the complement of a nucleotide sequence encoding a protein comprising SEQ ID NO:4,

(ii) the complement of a nucleotide sequence which is 95% identical to a nucleotide sequence encoding a protein comprising SEQ ID NO:4."

Claim 1 is directed to an isolated nucleic acid encoding a lipoprotein or active fragment thereof which mediates adhesion of Neisseria cells to human cells selected from SEQ ID NO:4, a nucleic acid having 95% sequence identity to a nucleotide sequence encoding the peptide sequence of SEQ ID NO:4 and a nucleic acid that hybridizes to a nucleic acid having a nucleotide sequence that encodes the peptide sequence of SEQ ID NO:4, under stringent conditions. This claim could not possibly be interpreted by one of ordinary skill in the art to encompass "an isolated nucleic acid sequence and/or any variant thereof that encodes a lipoprotein or any fragment thereof that mediates adhesion of Neisseria cells to human cells" as alleged by the Examiner.

The Examiner is referred to the guidelines for Written Description Requirement published January 5, 2001 in the Federal Register at Vol. 66, No. 4, pp. 1099-1110 (see

http://www.uspto.gov). The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by disclosure of relevant, identifying characteristics. (Federal Register, Vol. 66, No. 4 January 5, 2001). However, disclosure of one representative may describe a genus when all of the procedures for making the members of that genus are known. For example, according to the USPTO Written Description guidelines, "procedures for making variants of SEQ ID NO:X which have 95% identity to SEQ ID NO:X and retain its activity are conventional in the art." See Example 14: Product by Function. Further, methods for isolating nucleic acids via hybridization are also well known in the art. Therefore, the genus encompassed by claims 1 and 6 is adequately described in the specification.

Again, as evidence that the present claims fully comply with the written description requirements currently in practice at the USPTO, the Examiner is referred to claim 6 of the parent application, Meyer et al. Claim 6 of Meyer et al. represent current acceptable U.S. practice and is sufficiently similar to the language used in the present claim to be analogous. For instance, parts (b) and (c) of claim 1 are almost identical to parts (c) and (d) of claim 6 of Meyer et al. That is, both are directed to isolated nucleic acids that are 95% in identity to a SEQ ID NO and both are directed to isolated nucleic acids that hybridize under the same stringent conditions to the same a nucleic acid having the same SEQ ID NO as the prior part. Furthermore, the isolated nucleic acids of the present invention, as recited in the claims, clearly possess a biological function and are associated with a function that has been proven to exist. (*See, Id.* at, for instance, Example 4 and Table 1).

Thus, Applicants submit that claims 1-9 fully comply with the written description requirements of 35 U.S.C. § 112, first paragraph, and request rejections based on this statute be reconsidered and withdrawn.

Enablement

Determination of enablement is to be a weighing of several factors, as enumerated in *Ex parte Forman*, 230 USPQ 547 (BPAI 1986). The factors to be considered are: the quantity of experimentation necessary, the amount of direction or guidance provided by the specification, the state of the prior art, the presence or absence of working examples, the nature of the invention, the relative skill of the worker in the art, the predictability of the art and the scope of the claims. *In re Wands* 8 USPQ2d 1400 (Fed. Cir. 1988), affirms these factors and further holds that the quantity of experimentation demanded is not determinative, but the issue of whether undue experimentation is needed to practice the full scope of the invention rules. *Wands* further establishes that, if the making of variants and screening them for activity is expected in the art to identify those that are operable, such screening is not undue experimentation if the relevant screen is described in the specification or known in the art. *Wands* at 1406.

The Examiner fails to consider any of these factors, and merely states, "applicant's disclosure does not enable one skilled in the art to practice the invention as claimed without further undue amount of experimentation, which requires the identification and characterization of not only SEQ ID NO:4 but also nay and all variants of SEQ ID NO:4 like proteins for the role of the encoded protein in the adhesion of Neisseria cells to human cells." However, the Examiner does not explain what the test for enablement is, nor does the Examiner explain how

the present invention does not meet this test. The true issue is whether it is predictable that one of skill in the art, given one functional embodiment, can find another. Thus, the Examiner fails to establish a *prima facie* case for non-enablement and the rejection should be withdrawn on this basis alone.

Correct consideration of the *Forman* factors would reflect the following:

1. The invention is directed to cloned nucleic acids encoding a protein that has a defined structural characteristic, i.e. SEQ ID NO:4, or that has a recited biological activity, i.e. mediates adhesion of Neisseria cells to human cells.

2. The scope of the claims at issue is indeed generic, but constrained by either a stated degree of identity to a reference sequence or functionally by hybridization to a reference sequence under defined conditions. Some claims are limited functionally in terms of the biological activity of the protein encoded by the claimed nucleic acid.

3. Most practitioners in the art hold a Ph.D. and thus the skill of the practitioner is very high.

4. The specification provides description of essential features of the protein of the invention (SEQ ID NO:4) and of a nucleic acid encoding it as well as the complete open reading frame of one species of OrfA nucleic acid and biological activities associated with OrfA. Thus the specification provides considerable guidance as to structural requirements for functional embodiments. The specification further provides guidance in the form of an assay (Example 4) that can be used to test any particular embodiment for function.

5. The specification provides working examples of the isolation of nucleic acids encoding orfA protein and further provides a working example of an assay that can be used to determine if any particular embodiment possesses the biological activity recited in the claims.

6. The quantity of experimentation required to make variants of an nucleic acid is not large by the standards of the art. The specification discloses at least one cloned DNA encoding an entire OrfA protein, and kits are available commercially for performing mutagenesis along the entire length of the cloned DNA. Furthermore, the Specification clearly teaches the identification of other fragments. (*See*, Specification, at pages 10 and 14-15).

7. The quantity experimentation required to screen variants might be large, but again, not unexpected in the art. Variants can be screened by any of the assays known in the art and the necessity for screening of variants is expected in the art. For example, screening using hybridization techniques is known in the art and described in the specification.

8. While it is perhaps unpredictable whether any particular variant would have the biological activities ascribed to OrfA, it is very predictable that any given mutation-screening experiment will allow isolation of functional variants.

Applicants submit that proper consideration of the factors for weighing enablement will result in withdrawal of the instant rejection. For all of the above reasons, Applicants submit that the claimed invention should be considered enabled by the specification and the instant rejection should be withdrawn.

If the Examiner has any questions or comments, please contact Thomas J. Siepmann, Registration No 57,374 at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

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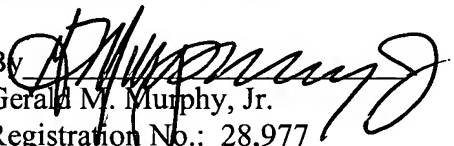
Respectfully submitted,

By 
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